REVIEW ARTICLE

Acute Ischemic Stroke Management Review for the Hospitalist

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The treatment of acute ischemic stroke is dependent on timely recognition. After ensuring airway, respiratory and circulatory stability, NIHSS should be performed and urgent CT scan obtained. If no exclusions exist, recombinant tissue plasminogen activator (rtPA) should be administered as soon as possible. Select patients may be eligible for mechanical thrombectomy. Stroke patients should be admitted to a dedicated stroke service to determine stroke mechanism, manage risk factors, and initiate preventive therapies.

INTRODUCTION

Epidemiology

800,000 strokes occur in the United States (US) each year with 80% being first time events (1). A large international study recently identified hypertension, lack of exercise and elevated serum lipids as the most significant risk factors for an acute stroke (2). Attention to these and other independent stroke predictors including diabetes mellitus, obesity, smoking and cardiovascular disease decreased stroke incidence in the last 30 years (3). Adoption of the Mediterranean diet alone can reduce first stroke events by 40% (4). The use of statins and antihypertensive medications correlates with a 40% decrease rate of stroke in Medicare patients older than the age of 65 (5). Recurrent stroke rates dropped from 9% in the 1960s to 5% in the 2000s with a projected rate of under 3% in the coming decade (6). Despite these trends, stroke remains the second leading cause of death worldwide, the fifth leading cause of death in the US and a primary cause of long-term disability (1,7).

Significant ethnic, gender and geographic stroke disparities exist. Although stroke is more common in men younger than 79 years old than in women (8), the lifetime risk of stroke is higher in woman due to a longer life expectancy (9). Stroke symptoms are more common in blacks than whites, and in those with lower economic and educational status (10). Although stroke incidence declined among white Americans between 1990 and 2005, stroke incidence in blacks remained unchanged (11). Black and Mexican Americans also have a higher incidence of both young age stroke and stroke-related deaths than white Americans (1,12). Reflecting this ethnic disparity, stroke mortality is 20% higher in the Southeast stroke belt of the US (13).

Pathophysiology

More than 85% of strokes are ischemic with the remainder being hemorrhagic (1). The Trial of ORG 10172 in the Acute Stroke Treatment (TOAST) etiologic classification system divides ischemic strokes based on their etiology as follows: large-vessel atherosclerosis, cardioembolic source, small-vessel disease, other determined causes, and cryptogenic (14). A recent analysis of an acute ischemic stroke confirmed by diffusion-weighted imaging

(DWI) in a large Asian cohort utilizing TOAST classification found large-artery atherosclerosis to be the most common stroke subtype with the middle cerebral artery (MCA) territory most frequently affected (15). However, a non-Asian population determined cardioembolic stroke to be the most common subtype (16). In fact, atrial fibrillation, the prevalence of which is estimated to rise to 12 million in the US by 2030, independently increases stroke risk five-fold across all ages (17,18).

Although stroke was once defined as the rapid development of disturbed cerebral function lasting at least 24 hours or leading to death (19), clinically "silent" strokes occur in 20% of healthy elderly patients (20), and one third of transient ischemic attacks result in an acute ischemic lesion on an MRI (21). The modern definition of stroke encompasses retinal, brain, or spinal cord ischemic cell death as defined by neuroimaging, neuropathology, or clinical examination (22).

How quickly clinical symptoms of a cerebral ischemia emerge following a vascular occlusion depends on the rate at which cerebral autoregulation fails to perfuse collateral blood vessels (23). Cerebrovascular hemodynamic compromise is first met by a compensatory increase in cerebral blood volume in order to maintain constant cerebral blood flow (24). After cerebral vasodilation is maximized, blood oxygen extraction increases in an attempt to maintain tissue viability. However, as this autoregulatory process is overwhelmed, cerebral blood flow decreases resulting in tissue hypoperfusion and the formation of an ischemic penumbra—tissue that is no longer metabolically functional although still viable (25). If perfusion to the penumbra is not increased in a timely manner, an ischemic core of irreversible cell death results.

Times is Brain

It is estimated that two million neurons die for every minute that reperfusion is delayed (26). Intravenous thrombolysis via recombinant tissue plasminogen activator (rtPA; alteplase) within 4.5 hours is safe and effective for many acute stroke patients (27-30). rtPA increases the likelihood of patient independence at three months and is now recommended equally for those younger and older than the age of 80 (27). However, its use is extremely time dependent (28). Every 30-minute delay in reperfusion by intra-arterial therapy decreases a good clinical outcome by 15% (29). The use of prehospital screening tools such as the Cincinnati Prehospital Stroke Scale or Los Angeles Prehospital Stroke Screen can readily identify stroke patients in the field. The Rapid Arterial Occlusion Evaluation (RACE) scale has also been shown to accurately identify patients with large arterial occlusion in the prehospital setting (30). The recent advent of formal telemedicine stroke guidelines (31) and the developing concept of mobile stroke units are addressing the profound problem of thrombolysis underutilization in acute stroke management (32). With the indisputable efficacy of endovascular thrombectomy (NNT = 2.6) and an intervention window of up to 7.3 hours, the opportunity to treat an acute ischemic stroke has never been greater (33,34).

DIAGNOSIS

Clinical Diagnosis

A patient suspected of having an acute stroke should be treated emergently. After ensuring respiratory and hemodynamic stability, it is crucial to confirm the time the patient was last known to be well. Knowledge of the last known well will determine if the patient is within the time window for an acute intervention. Although a general screening assessment may be performed by the nursing staff, it is most important that the National Institute of Health Stroke Scale (NIHSS) be performed.

NIHSS is a standardized assessment of level of consciousness, language, neglect/ extinction, visual fields, eye movements, facial symmetry, motor strength, sensation, and coordination as demonstrated in Table 1 (35). The NIHSS can be performed quickly by various healthcare providers, and the certification can be obtained online for minimal to no cost (36). Baseline NIHSS score <6 increases the likelihood of a good recovery while scores >16 increase the likelihood of a severe disability or death (37). A future outcome at 3 months is best predicted by the baseline NIHSS score. A cut off

score of 13 on the NIHSS reliably predicts patient independence (38).

Table 1. National Institutes of Health Stroke Scale (NIHSS)

1a. Level of Consciousness	0 = Alert; keenly responsive. 1 = Not alert; but arousable by minor stimulation to obey, answer, or respond. 2 = Not alert; requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped). 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, and areflexic.
1b. LOC Questions	0 = Answers both questions correctly. 1 = Answers one question correctly. 2 = Answers neither question correctly.
1c. LOC Commands	0 = Performs both tasks correctly. 1 = Performs one task correctly. 2 = Performs neither task correctly.
2. Best Gaze	0 = Normal. 1 = Partial gaze palsy; gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present. 2 = Forced deviation, or total gaze paresis not overcome by the oculocephalic maneuver.
3. Visual	0 = No visual loss. 1 = Partial hemianopia. 2 = Complete hemianopia. 3 = Bilateral hemianopia (blind including cortical blindness).
4. Facial Palsy	0 = Normal symmetrical movements. 1 = Minor paralysis (flattened nasolabial fold, asymmetry on smiling). 2 = Partial paralysis (total or near-total paralysis of lower face). 3 = Complete paralysis of one or both sides (absence of facial movement in the upper and lower face).
5. Motor Arm	0 = No drift; limb holds 90 (or 45) degrees for full 10 seconds. 1 = Drift; limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. 2 = Some effort against gravity; limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. 3 = No effort against gravity; limb falls. 4 = No movement. UN = Amputation or joint fusion, explain: _____ 5a. Left Arm 5b. Right Arm
6. Motor Leg	0 = No drift; leg holds 30-degree position for full 5 seconds. 1 = Drift; leg falls by the end of the 5-second period but does not hit bed. 2 = Some effort against gravity; leg falls to bed by 5

	seconds, but has some effort against gravity. 3 = No effort against gravity; leg falls to bed immediately. 4 = No movement. UN = Amputation or joint fusion, explain 6a. Left Leg 6b. Right Leg
7. Limb Ataxia	0 = Absent. 1 = Present in one limb. 2 = Present in two limbs. UN = Amputation or joint fusion, explain
8. Sensory	0 = Normal; no sensory loss. 1 = Mild-to-moderate sensory loss; patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick, but patient is aware of being touched. 2 = Severe to total sensory loss; patient is not aware of being touched in the face, arm, and leg.
9. Best Language	0 = No aphasia; normal. 1 = Mild-to-moderate aphasia; some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided materials difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content from patient's response. 2 = Severe aphasia; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = Mute, global aphasia; no usable speech or auditory comprehension.
10. Dysarthria	0 = Normal. 1 = Mild-to-moderate dysarthria; patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = Severe dysarthria; patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/ anarthric. UN = Intubated or other physical barrier, explain
11. Extinction and Inattention (formerly Neglect)	0 = No abnormality. 1 = Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 = Profound hemi-inattention or extinction to more than one modality; does not recognize own hand or orients to only one side of space.

The use of the NIHSS may help exclude stroke mimics (39). Several studies show that alternate diagnoses are found in 22 to 38% of suspected stroke cases (40-42). It is essential to distinguish stroke from notable mimics since rtPA administration not only exposes the patient

to unnecessary bleeding risk, but also costs more than $5400 on average (43). Notable stroke mimics include seizure, encephalopathy, syncope, migraine, sepsis, and toxic/ metabolic derangements (42). Compared to mimics, stroke is more likely if a patient has almost any focal neurological symptom, such as subjective hand weakness or objective hemiparesis (42). Stroke is also more common with a normal mental status, NIHSS 1b score of 0, admission to a cardiology service, atrial fibrillation at the time of onset or during hospitalization, history of prior stroke and obesity (40,42,44). In contrast, increased likelihood of a stroke mimic is seen with patients exhibiting objective confusion, known history of cognitive impairment, loss of consciousness, seizure at onset, retained ability to walk, and absence of lateralizing symptoms (40,42,44). In-hospital stroke alerts are typically activated by nurses or physicians when a patient's neurological status acutely changes from his/ her baseline. Nurses have been found to effectively identify in-hospital ischemic events and activate stroke alerts earlier (45).

Neuroimaging for Diagnosis

The non-contrast head CT scan remains the first-line imaging study in suspected stroke patients (46). The National Institute of Neurological Disorders and Stroke (NINDS) Brain Attack algorithm for stroke assessment recommends CT within the first 25 minutes of symptom recognition (46). It is readily available, quick and allows for timely rtPA administration within the recommended 3 to 4.5 hour window when indicated. Identifying hemorrhage is a fundamental step prior to rtPA administration since the thrombolytic therapy may produce lethal bleeding in patients with intracranial hemorrhage. Such bleed is recognized on CT as a hyperdense signal (46). An early CT finding of ischemia is a loss of gray-white matter differentiation in the basal ganglia or the insular cortex (insular ribbon sign). This is a time dependent sign, more likely to be visible at 6 hours after the stroke (46). CT also helps identify arterial occlusion with thrombus, which appears as a hyperdensity of the involved large artery (46,47). Typical locations are the M1 segment of the middle cerebral artery (hyperdense MCA sign), within the Sylvian fissure, basilar artery (dot sign), the posterior cerebral artery, or the anterior cerebral artery (46,47). This early finding may predict early deterioration, worse prognosis and greater risk of hemorrhage following thrombolysis (46). Distal MCA branch occlusions have less swelling and mass effect compared to internal carotid artery (ICA) and proximal MCA occlusions with less serious clinical implications (48).

Early hypoattenuation on a CT reflects severe hypoperfusion and possible irreversible damage (49). Detection of MCA territory hypodensity on hyperacute CT scans is a sensitive, prognostic, and reliable indicator of the amount of MCA territory undergoing infarction (50).VonKummar *et al* showed that less than 33% of the MCA territory parenchymal hypoattenuation predicted a good response to rtPA (51). Frank hypodensity within 6 hours or damage to one third or more of the MCA territory predicts poor prognosis and malignant edema (48). Other early parenchymal signs include attenuation of lentiform nucleus, hemispheric sulcal effacement and a midline shift (52). On the initial emergency CT scan, overt non-stroke processes must also be confidently excluded, such as tumor, subdural/ epidural hematoma, and a subarachnoid hemorrhage (46). Nevertheless, a non-contrast CT cannot definitively differentiate the ischemic core of irreversible cell death from the ischemic penumbra, which is at risk of infarction but salvageable by targeted reperfusion strategies. This crucial distinction is made by CT perfusion scanning with a sensitivity and specificity of more than 90% despite its limited spatial coverage (46,53). It is especially useful in wake-up strokes or strokes with undetermined time of onset (54).

CT angiography (CTA) is a rapid technique that allows extensive visualization of vessels from the aortic arch to the entire circle of Willis as well as the collaterals within seconds. It has 100% sensitivity and 82-100% specificity for identifying occlusions (46, 55-57). It is also superior to a carotid ultrasound in differentiating high grade carotid stenosis from an occlusion (58). Due to its high accuracy and speed, CTA is highly valuable in the rapid triage of hyperacute stroke patients to intra-arterial thrombolytic

treatment (59). CTA is also beneficial in recognizing large non-stenotic plaques, more common in the ipsilateral carotids, which are implied in cryptogenic strokes (60). Multiphase CTA is an imaging tool that provides three time-resolved images of pial arterial filling in the whole brain; it has excellent inter rater agreement, especially for anterior circulation occlusions (61,62). Multimodal CT evaluation improves detection rate and prediction of the final size of an infarction in comparison with unenhanced CT, CT angiography, and perfusion CT alone (63). The role of magnetic resonance imaging (MRI) in acute ischemic stroke is a topic of ongoing study. MRI can aid appropriate selection of patients who need endovascular therapy and decrease exposure to invasive procedures in inappropriate patients thus improving outcomes and patient safety (64).

TREATMENT

Currently the only USFDA approved medical therapy for an acute ischemic stroke within 3 hours of last known normal is intravenous rtPA. The recommended dose is 0.9 mg per kg body weight with 10% given as an initial bolus. The NINDS rtPA stroke study demonstrated a benefit of intravenous rtPA therapy for patients with ischemic stroke compared to placebo regardless of the stroke subtype. As compared to placebo, patients treated with rtPA were at least 30% more likely to have minimal or no disability at three months with no increase in mortality (65). Multiple trials have demonstrated a greater benefit when treatment is initiated within 3 hours of the onset of symptoms (66). Patients with NIHSS of 20 or more have an increased risk of a hemorrhagic transformation of the ischemia after rtPA (67). It is recommended that acute stroke patients be admitted to specialized, dedicated stroke units whenever possible as they are associated with a higher rate of timely administration of rtPA when compared to hospitals without stroke units (67).

Intravenous rtPA administration 3 to 4.5 hours after the onset of stroke symptoms is associated with a modest but significant improvement in the clinical outcome, without a higher rate of symptomatic intracranial hemorrhage than that reported among patients treated within 3 hours (65). Treating patients outside these times is associated with an increase of hemorrhagic complications and death (66). Additionally, the extended time window for rtPA (i.e., 3-4.5 hours from last known normal) has additional exclusion criteria. These include a prior history of stroke and concomitant diabetes, any PT/INR if history of anticoagulation use, NIHSS >25, and age > 80 years.

rtPA has a clear benefit in treatment in elderly stroke patients, those with severe stroke, those with diabetes mellitus and hyperglycemia, and those with minor early ischemic changes evident on computed tomography (27). The most common exclusion found for rtPA is delay in presentation to medical attention (69-71). Others include recent intracranial surgery, significant head trauma and on-going GI/ GU bleeding (27). The table shows the typical inclusion and exclusion criteria used prior to rtPA administration (Table 2) (27).

Table 2. Inclusion and exclusion criteria for rtPA within 3 hours from last known well following acute ischemic stroke

Inclusion criteria:
• Diagnosis of ischemic stroke causing measurable neurological deficit • Onset of symptoms<3 hours before beginning treatment • Aged ≥18 years
Exclusion criteria:
• Significant head trauma or prior stroke in previous 3 months • Symptoms suggest subarachnoid hemorrhage • Arterial puncture at noncompressible site in previous 7 days • History of previous intracranial hemorrhage • Intracranial neoplasm, arteriovenous malformation, or aneurysm • Recent intracranial or intraspinal surgery

- Elevated blood pressure (systolic >185 mm Hg or diastolic >110 mm Hg)
- Active internal bleeding
- Acute bleeding diathesis, including but not limited to
- Platelet count<100 000/mm³
- Heparin received within 48 hours, resulting in abnormally elevated Aptt greater than the upper limit of normal
- Current use of anticoagulant with INR >1.7 or PT >15 seconds
- Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and ECT; TT; or appropriate factor Xa activity assays)
- Blood glucose concentration<50 mg/Dl (2.7 mmol/L)
- CT demonstrates multilobar infarction (hypodensity>1/3 cerebral hemisphere)

Relative exclusion criteria:

- Recent experience suggests that under some circumstances—with careful consideration and weighting of risk to benefit—patients may receive fibrinolytic therapy despite 1 or more relative contraindications. Consider risk to benefit of IV rtPA administration carefully if any of these relative contraindications are present:
- Only minor or rapidly improving stroke symptoms (clearing spontaneously)
- Pregnancy
- Seizure at onset with postictal residual neurological impairments
- Major surgery or serious trauma within previous 14 days
- Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days)
- Recent acute myocardial infarction (within previous 3 months)

Notes:

- The checklist includes some FDA-approved indications and contraindications for administration of IV rtPA for acute ischemic stroke. Recent guideline revisions have modified the original FDA-approved indications. A physician with expertise in acute stroke care may modify this list.
- Onset time is defined as either the witnessed onset of symptoms or the time last known normal if symptom onset was not witnessed.
- In patients without recent use of oral anticoagulants or heparin, treatment with IV rtPA can be initiated before availability of coagulation test results but should be discontinued if INR is >1.7 or PT is abnormally elevated by local laboratory standards.
- In patients without history of thrombocytopenia, treatment with IV rtPA can be initiated before availability of platelet count but should be discontinued if platelet count is <100 000/mm³.
- aPTT indicates activated partial thromboplastin time; CT, computed tomography; ECT, ecarin clotting time; FDA, Food and Drug Administration; INR, international normalized ratio; IV, intravenous; PT, partial thromboplastin time; rtPA, recombinant tissue plasminogen activator; and TT, thrombin time

Some stroke patients may be eligible for mechanical embolectomy (72). Endovascular therapy with clot retrievers, revascularization devices, or endovascular rtPA administration have all shown to have better revascularization rates, outcomes and prognosis compared to IV rtPA alone (73). Studies have shown that endovascular thrombectomy is beneficial, especially in strokes of anterior circulation, in patients >80 years of age and may be useful in those not eligible for IV rtPA(33). Recent mechanical thrombectomy trials have shown improved functional outcomes in patients who received a combination of rtPA followed by mechanical thrombectomy (74-76). A meta-analysis showed that endovascular thrombectomy with medical therapy resulted in better outcomes at 3 months than medical therapy alone in large vessel strokes. The benefit was insignificant when thrombectomy was performed 7.3 hours after the symptom onset (34).

Decompressive hemicraniectomy may be necessary in patients with large ischemic stroke who develop malignant cerebral edema and decreased level of consciousness. It reduces mortality and is recommended in patients <60 years of age with unilateral MCA occlusion who deteriorate within 48 hours despite medical therapy. While it improves survival, most patients continue to have permanent disabilities (48).

INPATIENT CONCERNS

A limited number of hematologic, coagulation, and biochemistry tests are recommended during the initial emergency evaluation in patients with suspected ischemic stroke to identify systemic conditions that may mimic stroke, that cause stroke or that may influence therapeutic options. These tests include blood glucose, electrolytes, complete blood count with platelet count, prothrombin time, activated partial thromboplastin time, international normalized ratio, and renal function studies (39,77). A clinical cardiovascular examination, cardiac enzymes tests, and a 12-lead electrocardiogram (ECG) should be performed in all stroke patients (78). Abnormalities on the non-contrast head CT scan remains the first-line imaging study in suspected stroke patients due to its ubiquity and exquisite sensitivity for ruling out hemorrhagic strokes (46). On the initial CT scan, overt nonstroke processes, as previously discussed, must be excluded. Chest radiographs in patients with an acute stroke are not indicated in the absence of appropriate clinical indications with only 3.8% of all patients radiographed having alterations in management (79). Most patients with stroke do not need an examination of the cerebrospinal fluid except for an evaluation of a patient with a stroke that may be secondary to an infectious illness or a subarachnoid hemorrhage (39,77).

Airway and Ventilation

Prevention of an early aspiration and airway protection are essential aspects of inpatient stroke care. Cheyne-Stokes respiration is frequent in stroke patients. Supplemental oxygen is recommended if the patient is hypoxic with saturation <92% (39,80,81). Patients with decreased consciousness, absent corneal and light reflex, cardiomyopathy, and age >80 years have the greatest risk for poor airway protection (82-84). Patients with an MCA stroke who require mechanical ventilation have high mortality regardless of the cause of intubation. The survival is associated with incomplete MCA territory involvement and atherosclerosis origin (85). Endovascular studies have noticed that patients who require general anesthesia have worse functional outcomes at 90 days versus those who do not require general anesthesia as part of their acute care (86).

Cardiac Monitoring

The most common arrhythmia detected in the setting of a stroke is atrial fibrillation. Common ECG changes secondary to a stroke with left-sided neurological events include an ST-segment depression, QT dispersion, and a prolonged QT interval (87-89). Therefore, guidelines recommend patients with an acute ischemic stroke should have cardiac monitoring for at least the first 24 hours and treatment of any serious cardiac arrhythmias that arise.

NEURO ICU MANAGEMENT

Pressure Augmentation

The ischemic penumbra is the collaterally perfused area surrounding the infarct in a setting of impaired autoregulation wherein the impaired blood flow is insufficient for normal neuronal function, but sufficient for cell viability (90). Elevated blood pressures following an ischemic stroke serve to preserve perfusion to the penumbra and this is the rationale behind pressure augmentation (91). Blood pressure is increased in a step wise manner using IV vasopressors and regular neurological examinations guide escalation end-points as well as weaning of augmentation (39,77,91). Multiple perfusion imaging studies have demonstrated that an elevation in blood pressure with phenylephrine partially restores perfusion to the penumbra. (90,92-95). Rordorf *et al*. showed that maintaining a mean systolic blood pressure of 156 mm Hg (range 120 to 190 mm Hg) proved clinically beneficial (94). Wityk *et al.* also demonstrated improvements in perfusion imaging by maintaining the systolic blood pressure 20-30% above baseline (96,97). Ischemia can be identified by changes in tissue metabolism and oxygenation by monitoring brain tissue oxygen tension and microdialysis (91). Continuous EEG monitoring is noninvasive and demonstrates higher prevalence of slower frequencies with decreased cerebral blood flow (91). Other treatment options include withdrawing previous antihypertensive therapy and augmenting intravenous fluids. Historically,

it has been thought that keeping the head of the bed as flat as possible might improve cerebral perfusion; however, this theory has been recently challenged (98).

POST rtPA CARE

Blood Pressure

Blood pressure is found to be elevated in most patients on the day of admission and such early elevation is thought to be a physiological response to ischemia. Patients with preexisting hypertension with moderately elevated pressures may not require antihypertensive therapy as it can impair cerebral blood flow and lead to neurological deterioration (99). rtPA is given only if blood pressure is less than 185/110; it should be maintained at that level for the first 24 hours after rtPA administration (39,77). For patients who do not receive rtPA, the American Heart Association/ American Stroke Association (AHA/ASA) guidelines recommend initially withholding antihypertensive treatment unless the blood pressure is greater than 220/120 (39,77).

Temperature

Hyperthermia acts through several mechanisms to worsen cerebral ischemia, some of which include enhanced release of neurotransmitters, exaggerated oxygen radical production, and worsening of cytoskeletal proteolysis (100). A temperature greater than >37.9°C within the first week after the stroke was an independent predictor of a poor outcome (101,102). Lowering an acutely elevated temperature greatly influences outcome and prognosis (103). Therefore, guidelines suggest that sources of fever should be treated, and antipyretic medications should be administered to lower the temperature in febrile stroke patients.

Glucose

There is a correlation between an admission glucose concentration, diabetes, and poor stroke outcomes, which may not be attributed to the stroke type or location. Increased mortality was evident in the hyperglycemic and diabetic groups (104). Hyperglycemia is associated with lactic acidosis and conversion of penumbral tissue to an infarction, greater final infarct size, and worse functional outcome (104). These correlations were independent of baseline stroke severity, lesion size, and diabetic status (105). Insulin therapy benefits transient focal ischemia (106). Serum glucose concentrations 140-180 mg/dL should probably trigger administration of insulin (77). Persistent hyperglycemia, as measured by serial blood glucose levels, is indicative of infarct evolution and worse clinical outcome regardless of baseline stroke severity than an isolated measure of glucose on admission to hospital (107).

Antiplatelet/ Anticoagulation

Two large trials studying the effects of aspirin and heparin in an acute stroke, the Chinese Acute Stroke Trial (CAST) and the International Stroke Trial (IST), have shown that starting aspirin as early as possible prevents stroke recurrence (108,109). AHA/ ASA guidelines recommend a dose of 325 mg orally within 48 hours of an acute stroke (39,77). The use of anticoagulation is not recommended in the acute setting because of the risk of hemorrhagic transformation (108,109,110,111).

DVT Prophylaxis

Incidence of deep-vein thrombosis (DVT) in stroke patients is comparable with that seen in patients undergoing a hip or knee replacement with multiple risk factors for DVT, like advanced age, low Barthel Index severity score, or hemiplegia (112). As pulmonary embolism is found to be responsible for approximately 10% of deaths following an acute stroke, the prevention of this complication is of crucial importance (39,77). Prospective trials have shown that early heparin treatment with low molecular weight heparin (LMWH) is effective in reducing DVT and pulmonary embolism in stroke patients (112,113). Current guidelines recommend subcutaneous LMWH for DVT prophylaxis (39,77).

HOSPITAL GOALS

Etiology Workup

The etiology of a stroke is determined based on clinical features and various diagnostic tests. Cardiac imaging with echocardiography is invaluable in an acute diagnosis (114). If

echocardiography is unrevealing and no arrhythmias are detected on telemetry during hospitalization, extended outpatient rhythm monitoring should be considered (115). Rare causes of stroke include non-atherosclerotic vasculopathies, hypercoagulable states, or hematologic disorders (14). Hypercoagulable etiological workup is necessary in younger stroke patients (116-118).

Secondary Prevention

Secondary prevention focuses on preventing recurrence of cerebrovascular events. Hypertension is a major correctable risk factor for stroke. Treatment of hypertension has been shown to reduce the incidence of primary and secondary strokes (119). A reduction in diastolic BP of 5 mm Hg is associated with one third lower risk of stroke (120). There is a high risk of recurrence of transient ischemic attacks and minor ischemic strokes due to atherosclerotic intracranial arterial stenosis and lacunar strokes (121-123). Dual antiplatelets, like aspirin with clopidogrel, may be necessary in some patients (121-123). If no contradictions are present, ischemic stroke/ transient ischemic attack patients with atrial fibrillation are anticoagulated long-term with warfarin or a newer oral anticoagulant (124). Identification of an aortic atheroma may prompt therapy with aspirin, statins and/ or anticoagulation to prevent recurrent strokes (125,126). Using statins in such patients decreases the likelihood of a subsequent stroke (127). Patients with an ejection fraction of < 30% and a predicted 5 year survival tend to do better if anticoagulated (128). The timing for starting anticoagulation is individualized to each patient and is dependent on size of the ischemia, etiology of the ischemia, and other risk factors.

Recovery

Stroke patients have a high incidence of dysphagia ranging from 51 to 78% (129). All stroke patients require a bedside dysphagia screen (39,77). In case of ongoing aspiration, a percutaneous gastrostomy is recommended. Lastly, an evaluation by physical and occupational therapists is necessary for disposition for rehabilitation.

Outcomes

The modified Rankin Scale (mRS) is a valid measure of disability and defines 6 grades of disability as demonstrated in Table 3 (130). A scale of 0-2 indicates mild disability; a scale of 3 indicates moderate disability; scores of 4 or 5 indicate severe disability; and a score of 6 denotes death (130,131). It is employed to assess recovery from stroke after rtPA. A score of 0 or 1 at 3 month follow-up is considered a favorable outcome, whereas a score of 2-6 represents an unfavorable outcome (65). The scale is found to have satisfactory inter-rater agreement and is widely used as an outcome parameter in clinical trials of stroke treatments (130,133,134).

CONCLUSION

Successful treatment of acute ischemic stroke depends on rapid diagnosis and determination of rtPA/ endovascular intervention candidacy.

Table 3. Modified Rankin Scale (mRs)

Grade	
0	No symptoms at all
1	No significant disability: despite symptoms, able to carry out all usual duties and activities
2	Slight disability: unable to perform all previous activities but able to look after own affairs without assistance
3	Moderate disability: requiring some help but able to walk without assistance
4	Moderately severe disability: unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability: bedridden, incontinent and requiring constant nursing care and attention
6	Death

Notes

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